can be found on page 11, lines 19-28, to page 12, lines 1-5, and support for the amendment of claim 70 can be found on page 32, lines 1-2; and page 6, page 41, lines 23-24. Moreover, a spelling mistake in claim 70 has been corrected.

1. Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 43, 49-51, 54-55 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a composition according to the invention comprising a tumor cell conjugate and an adjuvant, allegedly does not provide enablement for a composition comprising the tumor cell conjugate alone.[1] In particular, the Examiner states (Office Action, p. 8) (emphasis added):

> Based on the teachings [as described] above and in the specification one of skill in the art would not expect that the claimed composition could be used as contemplated for the treatment of malignant tumors without specifically including an adjuvant as demonstrated in the specification.

Applicant respectfully disagrees with this reasoning. The haptenized tumor cell composition, as set forth in claim 43, is enabled by the disclosure. The Examiner does not contend that tumor cells cannot be obtained or haptenized. As such, the claimed composition is enabled. Moreover, the composition is a useful component of a vaccine or to be employed in a therapeutic method, as exemplified in the specification (see page 12, lines 23-25: "The compositions of the invention may be employed in the method of the invention singly or in combination with other compounds"; page 14, lines 7-8: "The composition may be mixed with an immunological adjuvant and/or a pharmaceutically acceptable carrier").

[1] See Office Action, page 7, paragraph 10.

The Examiner agrees that the specification enables a haptenized tumor cell composition, in combination with an adjuvant, for use in an immunotherapy of cancer. For this to be true, both components of an immunotherapeutic vaccine, in this case haptenized tumor cells and an adjuvant, must each be enabled.

This rejection, then, appears to turn on the Examiner's contention that a final vaccine product - haptenized tumor cells and an adjuvant - is useful, but the active immunospecific ingredient does not have an enabled utility. As pointed out above, the Examiner concedes that the active immunospecific ingredient, haptenized tumor cells, are enabled. Use of this composition, for example, in combination with an adjuvant for immunotherapy of cancer, is enabled. The utility of the haptenized tumor cells to prepare a vaccine composition for such immunotherapy, must be enabled.

Because the Examiner's enablement rejection turns on only the issue of usefulness (utility) of the composition itself, proof that the composition is useful obviates the enablement rejection. See M.P.E.P. § 2107 (Rev. I, Feb. 2000, p. 2100-28). There can be no doubt that the claimed composition - hapten modified tumor cells - is useful, e.g., to prepare a vaccine composition or for administration to a cancer patient with an adjuvant. Viewed in this light, the specification enables the claimed composition as a component for the ultimate therapeutic vaccine or use.[2] "Products are useful if they serve as starting materials or intermediates in producing other materials or articles which are directly useful". *Reiners v. Mehltretter*, 111 USPQ 97, 100 (CCPA 1956); cf.

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[2] In practice, the patient's tumor or tumor cells will be sent to a processing facility after resection for storage. Each vaccine dose is prepared by thawing the cells, haptenizing the cells, and shipping the haptenized cells to the patient's physician. The physician prepares and administers the vaccine, e.g., by mixing the cells with adjuvant prior to injection. Haptenized tumor cells are clearly a useful product as supplied to the physician for further preparation and administration.

In re Kirk and Petrow, 153 USPQ 48, 56 (CCPA 1967) ("... compounds employed as intermediates to produce other *directly* useful compounds were found to be themselves useful [citing *Reiners*]"). The Examiner errs in interpreting these claims as requiring adjuvant. See *Carl Zeiss Stifting v. Renishaw Pk*, 20 USPQ2d 1094, 1100 (Fed. Cir. 1991) (finding error in a claim interpretation that required a component of a device to operate like the device). Indeed, it is well settled that an invention need only be useful to some extent and in certain applications. Id., citing *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984).

The Examiner has also rejected claim 70 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not contain a written description of cyclophosphamide being administered "only" prior to the first administration.[3]

Claim 70 has been amended to more particularly point out and distinctly claim that which the Applicant regards as the invention (see discussion, *infra*). The term "only" is no longer recited in the claim, thus obviating this rejection.

Accordingly, Applicant believes that the above rejections should be withdrawn.

2. Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 57, 66, and 70 for allegedly being indefinite.[4] The Examiner contends that there is no antecedent basis for the term "cancer" in claims 57 and 66, and that claim 70 lacks antecedent basis for the phrase "wherein said therapeutically effective amount of cyclophosphamide".

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[3] See Office Action, page 8, paragraph 11.

[4] See Office Action, page 9, paragraph 12.

In response, applications have amended claims 57 and 66 to call for methods wherein the ***malignant tumor*** is from a ***cancer*** selected from the recited group of cancers. Support for these amendments can be found on page 11, lines 19-28, to page 12, lines 1-5.

Claim 70 has been amended to recite a method further comprising administering a therapeutically efficient amount of cyclophosphamide prior to the first administration of the tumor cell composition. Support for this amendment can be found, *e.g.*, at page 15, lines 12-20 and Example 1 (page 19, lines 2-5); Example 2 (page 21, lines 23-24); Examples 5 (page 32, lines 1-2) and 6 (page 41, lines 23-24). Moreover, the misspelling of "cyclophosphamide" in claim 70 has been corrected.

Accordingly, Applicant respectfully submits that the rejection should be withdrawn.

3. Rejections Under 35 U.S.C. § 103

The Examiner has rejected claims 47 and 65-77 [5] under 35 U.S.C. § 103 as allegedly being unpatentable over Murphy et al. (Lab Invest 1990;62:70A; hereinafter "Murphy"), in view of U.S. Patent No. 5,702,704 (hereinafter "'704 patent"), U.S. Patent No. 5,626,843 (hereinafter "'843 patent), U.S. Patent No. 5,008,183 (hereinafter "'183 patent"), or U.S. Patent No. 4,232,001 (hereinafter "'001 patent") (hereinafter collectively "the Antibody Patents"); and Geczy *et al.* (J Immunol. 1970;19:189-203, hereinafter "Getzy").[6]

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[5] The Examiner has newly rejected claim 77 for the same reasons as those advanced for maintaining the rejections of claim 47 and claims dependent thereon. Accordingly, in the interest of economy, all such related rejections are considered together.

[6] See Office Action, page 2, paragraph 5, and page 9, paragraph 13.

The Examiner has also rejected claims 47 and 65-77 under the same paragraph as allegedly being unpatentable over Berd '89 in view of the Antibody Patents and Geczy.[7]

Furthermore, the Examiner has rejected claims 43, 44, 47, and 49-77 as allegedly being unpatentable over Berd '89 in view of the Antibody Patents, Geczy, in further view of combinations of additional (mostly cumulative) references (Wiseman et al., West J Med 1989;151:283-288, hereinafter "Wiseman"; Berd et al., PASCO 1983;2:56, hereinafter "Berd '83; Sanda et al., J Cellular Biochem 1993;suppl.17D:120, hereinafter "Sanda"; and Moody et al., J Urol 1991;145:293A, hereinafter "Moody") aiming to substantiate additional features.[8]

Because the core set of references, Berd '89, the Antibody Patents, and Geczy, fails in all respects to render the claimed invention obvious, they are addressed prior to considering each of the obviousness rejections in turn.

a. The legal test for obviousness

A finding of obviousness under §103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. See Graham v. John Deere, 383 U.S. 1 (1966). A proper analysis of obviousness under §103 requires consideration of two factors: 1) whether the prior art suggests the claimed invention and 2)

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[7] See Office action, page 3, paragraph 6; and page 10, paragraph 14.

[8] See Office action, page 4, paragraph 7; page 6, paragraph 8; page 7, paragraph 9; page 10, paragraph 15; and page 11, paragraphs 16 and 17.

whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. See In re Vaeck, 947 F.2d 488, 493, 20 U.S.P.Q.2d (Fed. Cir. 1991)(citing In re Dow Chemical Co., 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988)). Both the suggestion and the reasonable expectation of success must exist in the prior art and not in the Applicant's disclosure. Id.

In order for a combination of prior art references to suggest a claimed invention, so as to render it obvious, an objective teaching must exist in the prior art that would lead a skilled artisan to combine its teachings. See In re Fritch, 972 F.2d 1260, 1266, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992)(citing In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988)). As the Federal Circuit has explained, "[o]bviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so." See Fritch, 972 F.2d at 1266, 23 U.S.P.Q.2d at 1783. Furthermore, "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to pieced [*sic*] together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that 'one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecated the claimed invention.'" Id.(quoting In re Gorman, 933 F.2d 982, 987, 18 U.S.P.Q.2d 1885 (Fed. Cir. 1991) and In re Fine, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988).

If the prior art does contain an objective teaching that provides an incentive or motivation to combine the art, this alone will not render a claimed invention obvious. The prior art must also provide a reasonable expectation of success for achieving the claimed invention in order

to render the invention obvious. See In re O'Farrell, 853 F.2d 894, 903, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988).

The Examiner alleges that Applicant's arguments in support of patentability in the previous amendment have been considered. However, certain statements by the Examiner suggest that this is not the case. In particular, the Examiner correctly states that "teachings of references can only be combined if there is some suggestion or incentive to do so [which must be found in the references]" (Office Action , p. 2) then erroneously states that "the test for obviousness is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art" (Office Action, p. 3). Thus, the Examiner seems to gloss over the threshold issues: whether the references can be combined and whether there is a reasonable expectation of success. As discussed above, where these elements lack, obviousness does not obtain.

The Examiner further incorrectly alleges that Applicants argue limitations not recited in the claim. However, with respect to claims 43 and 44, these claims recite that "said malignant tumor is not melanoma." With respect to claim 47, this claim requires "administration at least six times at spaced apart intervals." As shown in detail below, the references cannot be combined as suggested by the Examiner, and even if combined contain no teaching or suggestion of these claim elements. Thus, the claims are patentable over the references.

Applicant also takes issue with the Examiner's contention that "Applicant has argued and discussed the references individually without clearly addressing the combined teachings" (Office Action, p. 3). Each reference must be considered in its entirety. *W.L. Gore & Assoc., Inc. v. Garlock*, 220 USPQ 303 (Fed. Cir. 1983). Such consideration must evaluate (1) whether the

reference can properly be combined with the other references, and (2) whether the combination suggests the claimed invention with a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1988). The previous amendment does both.

b. The core references

i. Berd teaches only melanoma vaccines

The Examiner states that Berd teaches treatment of melanoma patients wherein a low dose of cyclophosphamide is administered prior to autologous vaccine.

Berd teaches the treatment of melanoma patients with a ***single*** injection of a vaccine comprised of autologous, irradiated melanoma cells conjugated to DNP and mixed with BCG preceded by low dose cyclophosphamide (300 mg/M^2).

Berd does not teach or provide any reasonable expectation of success in achieving treatment for any tumor, and particularly for treating lung cancer, colon cancer, breast cancer, kidney cancer, and prostate cancer, as claimed in claims 43 and 44. Nor does Berd contain any objective teaching that would suggest to one of skill in the art to administer the vaccine six times at spaced intervals, as claimed in claim 47. The other references cited by the Examiner do not supply the missing teaching, for the reasons set forth below.

ii. The Antibody Patents teach routine production of antisera

The Examiner states that the '704 patent, '843 patent, '183 patent, and '001 patent teach conventional immunization schedules wherein antigen is administered at least six times at spaced intervals. Indeed, the '183 patent teaches an assay for detecting the presence or absence of

antibodies that bind to a human retrovirus antigen. The '001 patent teaches non-human antibodies to estrophilin. The '843 patent teaches the use of antibodies as immunosorbents for the treatment of AIDS. The '704 patent teaches antibodies that recognize advanced glycosylation endproducts and methods of using the antibodies for the measurement of the amount of advanced glycosylation end products in plants, animals, and cultivated and synthesized protein material. None of these patents contains an objective teaching of the use of antibodies for the treatment of human cancers. Even if these patents did teach antibody-based (passive) immunotherapy, Applicant submits that such teaching would have no bearing on the present invention, which concerns active specific immunotherapy to tumors.

As the Examiner has noted, these patents teach conventional methods for generating an antigen specific antibody response. Such antibodies are useful as diagnostic reagents. The immunized subjects do not develop protective immunity to the immunogen; that is not the intention or the outcome. Thus, one might conclude that by following the teachings of these patents, one would be unlikely to generate a protective immune response. On the contrary, one could expect to generate an ***anti-hapten*** antibody response. Since the residual tumor cells against which anti-tumor immunity is desired do not carry hapten, these references are of no moment to the claimed invention. Thus, there is no nexus between any of these references and the claimed invention, and they add nothing to Berd.

Furthermore, these references do not teach or suggest at least six administrations or immunizations of haptenized tumor cells (or any pathogenic antigen) to humans at spaced intervals for the treatment of cancer. No objective teaching thus exists in these patents that would suggest to or motivate one of skill in the art to administer antibodies to humans at least six times at spaced

intervals in order to treat cancer. Picking isolated teachings of these references to reach such a conclusion demands hindsight gained from the instant application. As noted above, it is well settled that the references must contain the motivation for their combination with other references, and that hindsight is an improper basis for such a combination.

iii. Geczy only teaches contact DTH reagents

The Examiner states that Getzy teaches that halogenated dinitrobenzenes such as 1-chloro- and 1-fluoro-2,4-dinitrobenzene are commonly used to elicit delayed hypersensitivity. Applicant agrees. Indeed, there is no contention that contact reagents, which haptenize proteins, are well known in the art, and that a large number of such agents can be used as haptens in the practice of the present invention (*see, e.g.*, the specification at page 15, lines 6-9). The Examiner further alleges that CDNB and FDNB are equivalent. This is true; both reagents are capable of producing DNP haptens.

However, Geczy proposes that direct conjugation of DNFB with lymphocytes is necessary for transformation of the lymphocytes (Geczy, page 202, 4th full paragraph). In contrast, the present invention discloses that haptenization of tumor cells permits development of an effective anti-tumor response. Such a result appears to contradict Geczy's teachings, and thus is surprising and unexpected in view of this reference. To the extent that Geczy's teachings relate to Berd, they diverge and teach awy, precluding the core combination proposed by the Examiner.

To the extent that Geczy describes dinitrobenzene reagents, it is merely cumulative to the Berd reference discussed above. It adds nothing to the teaching of that reference.

d. The rejection over Murphy, Berd, Geczy, and the Antibody Patents

The Examiner has rejected claims 47 and 65-77 as allegedly unpatentable over Murphy *et al.* (Lab Investigation 62(1):70A, 1990; hereinafter "Murphy") in view of the Antibody Patents, Berd, and Geczy.

By incorporating, on page 5 of the Office Action, the reasons set forth in the previous Office action, the Examiner states that Murphy teaches a method for treating melanoma comprising sensitizing with DNCB, administering a therapeutically effective amount of cyclophosphamide, and administering a therapeutically effective amount of autologous, irradiated DNP-conjugated melanoma cells mixed with BCG. With respect to these teachings, Murphy is cumulative to Berd, which discloses each of these elements. The Examiner concedes that Murphy does not teach a method wherein a vaccine is boosted at least six times at spaced intervals, wherein cyclophosphamide is administered, wherein there is prior sensitization with 1-fluoro-2,4-nitrobenzene, or wherein at least one of the following is elicited upon administration to patients with an adjuvant: an inflammatory immune response against the tumor; a delayed-type hypersensitivity response against the tumor; activation of T lymphocytes that infiltrate the tumor, or activation of T lymphocytes that infiltrate the tumor where the lymphocytes are predominately CD8+CD4-.

The Examiner concludes that it would have been *prima facie* obvious to combine the methods of Murphy and the cited Antibody Patents because it is conventional to repeat antigen administration at least six times at spaced intervals. The Examiner further concludes that the claimed method is "anticipated" (sic obvious) because the method would inherently lead to an inflammatory immune response against a tumor, a delayed-type hypersensitivity response against the tumor, activated T lymphocytes that infiltrate the tumor, and activated T lymphocytes that infiltrate

the tumor in which the lymphocytes are predominately CD8+CD4-. The Examiner further concludes that it would have been *prima facie* obvious to use a dose of 300 mg/M^2 of cyclophosphamide in the method of Murphy because Berd teaches that dose is therapeutically effective in a method that uses the same haptenized melanoma cells with the same population of patients. The Examiner finally concludes that it would have been *prima facie* obvious to substitute DNFB for the DNCB of Murphy because Getzy teaches that dinitrobenzenes such as 1-chloro- and 1-fluoro-2,4-dinitrobenzenes are commonly used to elicit delayed hypersensitivity. The Examiner states that the burden is on the Applicant to prove that the method of the prior art does not result in prolonged survival of the patient and is functionally different than the method taught by the prior art.

In response, Applicant respectfully points out that for the reasons set forth above, the Examiner's rejection fails to establish *prima facie* obviousness. In short, Murphy and/or Berd fail to teach an effective method of treatment for treating a malignant tumor in a human patient as set forth in claim 47, i.e., by administering the haptenized tumor cell composition at least six times. The Antibody Patents, which as the Examiner concedes merely teach conventional methods for generating antibodies for immunoassays or immune binding, provide no missing teaching. Similarly, Geczy fails to provide any teaching pertinent to the claimed compositions and methods. It merely reports well known observations about contact antigens, and proposes a mechanism by which they transform responding lymphocytes.

In the instant Office Action, the Examiner also contends that (a') "the test for obviousness is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art"; (b') the combined teachings were not "clearly addressed"; (c')

multiple immunizations are conventional in the art for producing "all forms of immune response"; and (d') Geczy teaches the equivalence of CDNB and FDNB.

Applicants have already addressed Examiner's statements (a')-(d') (*see supra*).

Accordingly, considering all of the references for what they fairly teach or suggest in combination, this rejection is in error and should be withdrawn.

e. The rejection over Berd, the Antibody Patents, and Geczy

The Examiner has rejected claims 47 and 65-77 as allegedly unpatentable over Berd, the Antibody Patents, and Geczy.

For the reasons discussed in detail in (d) above, this rejection is in error and should be withdrawn.

f. The rejection over Berd, the Antibody Patents, and Geczy in view of Wiseman

The Examiner has rejected claims 43, 44, 47, and 49-76 as unpatentable over Berd, the Antibody Patents, and Geczy, and further in view of Wiseman. The Examiner states that Berd teaches that treatment of melanoma patients with autologous vaccine preceded by low dose cyclophosphamide induces DTH to melanoma cells and regression of metastatic tumors. The Examiner further states that one would have an expectation of success since it was already known that immunization with tumor cells alone, after pretreatment with cyclophosphamide, resulted in regression of metastatic tumors.

Moreover, the Examiner contends that Wiseman teaches that treatment of patients with lung, colon, and kidney cancer with autologous tumor cell vaccine preceded by

cyclophosphamide leads to prolonged survival. The Examiner then concludes that it would have been ***expected*** [emphasis added] that vaccines using other types of tumor cells would behave in a mechanistically similar manner to Berd's melanoma vaccine, since there were no teachings of any distinguishing features of melanoma cells making a difference in the immune response to a melanoma cell.

Applicant respectfully disagrees. Contrary to the Examiner's allegations, it is ***not*** expected that "vaccines using other types of tumor cells, shown to effectively treat cancer, would behave in a mechanistically similar manner to the melanoma vaccine described in Berd et al.". (See, Office action, page 5, lines 12-14). In the PTO-1449 form filed by Applicant on December 1, 1998, Applicant brought the Examiner's attention to Hanna et al. (U.S. Patent No. 5,484,596, hereinafter "Hanna").[9] Hanna teaches a method for the treatment of human colon cancer that involves the use of a vaccine which is made from irradiated human tumor cells.[10] The Examiner is requested to note that the Hanna et al. vaccine strategy appears to be effective ***only*** for treating colon cancer. A publication reporting on a clinical trial of the "Hanna et al." vaccine concedes that the vaccine was not effective for rectal cancer (Hoover et al., J. Clin. Oncology 11: 390-399, 1993; copy attached as Exhibit 1). Hoover et al. states that ". . . no benefits were seen in patients with rectal cancer who received [active specific immunotherapy with an autologous tumor cell-BCG vaccine]" (see Abstract; see also page 399, first column). Hence, although the Hanna vaccine was successful in

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[9] To this date, the Examiner has actually not returned said PTO-1449 form, and Applicant cannot therefore assume that the Examiner has, in fact, considered this reference in the evaluation of the instant invention.

[10] Hanna does not teach or suggest the haptenization of the tumor cells that comprise the vaccine.

treating colon cancer, it failed to provide any benefits to patients with rectal cancer, a tumor type closely related to colon cancer. Accordingly, even had Berd '89 successfully treated melanoma patients with his haptenized tumor cell vaccine, and not only provided preliminary and essentially anecdotal results relating to DTH-responses, it could not have been reasonably expected that a similar vaccine would be equally effective in the treatment of related tumors, much less tumors of completely unrelated origin.

Wiseman does not supply the missing teaching. Instead, Wiseman teaches an alternative form of immunotherapy that depends on the route of administration: intralymphatic immunization. This alternative, which Wiseman reports favorably, in no way suggests a deficiency or problem that would lead one of ordinary skill in the art to seek an alternative immunization strategy. On the contrary, it leads away from the claimed invention, thus precluding combining this reference in making the rejection.

Further, as discussed above, there is no reasonable expectation of successfully implementing the vaccination program described with respect to melanoma in Berd to other tumor types. This reference provides "preliminary" results that "may represent a significant advance in the immunotherapy of human melanoma." Hence, it lacks any reasonable expectation of an effective treatment for melanoma in particular, much less other tumors in general.

Thus, the references lack any objective teaching to combine their disclosures. Moreover, even if combined, the lack of any reasonable expectation of success as the disclosure of Berd '89 precludes determining that the invention is obvious. Accordingly, the Examiner's rejection is overcome and should be withdrawn.

g. The rejection over Berd, the Antibody Patents, Geczy, and Berd 1983

The Examiner has rejected claims 43, 44, 47, and 49-77 as allegedly unpatentable over Berd, the Antibody Patents, Geczy, and Berd *et al* (Proc. Am. Soc. Clin. Oncol. 1983, 2:56; hereinafter "Berd 1983"). Berd, the Antibody Patents, and Geczy are discussed above. The Examiner states that Berd '83 teaches treatment of breast cancer patients with autologous vaccine, and that the substitution of the breast cancer cells of Berd 1983 for the melanoma cells of Berd (1989) was *prima facie* obvious.

Applicant submits that the teaching of Berd '83 is cumulative to the teaching of Berd, which also discloses administration of cyclophosphamide three days prior to immunization with the autologous cell vaccine. Berd '83 does not supply any of the other missing teaching. In particular, this reference fails to provide any teaching providing an incentive to prepare a haptenized tumor cell vaccine or methods of ***treating*** cancer using such a vaccine. The mere mention of treating a breast cancer patient fails to overcome the missing teaching, particularly since this abstract lacks any suggestion that the cyclophosphamide pretreatment provided any therapeutic benefit to any of the patients, much less elicited a DTH response in the breast cancer patient. Accordingly, the combined references continue to lack any reasonable expectation of success.

In view of the foregoing remarks, Applicant submits that this rejection is in error and should be withdrawn.

h. The rejection over Berd, the Antibody Patents, Geczy, and Sanda and Moody

The Examiner has rejected claims 43, 44, 47, and 49-77 as allegedly unpatentable over Berd, the Antibody Patents, Geczy, further in view of Sanda *et al.* (J. Cellular Biochem. Suppl.

17(D):120; hereinafter "Sanda") and Moody *et al.* (J. Urol. 1991, 145:293A). Berd, the Antibody Patents, and Geczy are discussed above. The Examiner states that in particular Berd supplies the motivation to "decorate the tumor cells with hapten." Moreover, by referring, on page 7, to the reasons set forth in the previous Office action, the Examiner states that Moody teaches that lymphokine-transfected prostate cells generate an anti-tumor effect *in vivo*, and that Sanda addresses the feasibility of gene therapy for human prostate cancer. These references appear to be relevant because they suggest methods of anti-prostate cancer therapy.

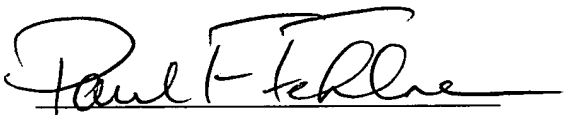
The deficiencies of Berd, the Antibody Patents, and Geczy have been discussed above. Applicant respectfully submits that Sanda and Moody fail to supply the missing teaching of the primary group of references. Indeed, both Sanda and Moody propose an alternative cancer therapy, in which the tumor cells are modified to express immunostimulatory cytokines. This is a divergent form of treatment: gene therapy. While Sanda merely reports the ability to transfect tumor cells with a retrovirus vector, Moody reports that prostate cancer cells that secrete IL-2 provide protection from an otherwise lethal tumor, and give short-lived protection against subsequent challenge. Neither reference suggests that there is a deficiency, or provides any motivation to decorate the tumor cells with hapten in order to elicit an effective immune response. Thus, they add nothingto the other references, which are deficient for the reasons already advanced. Moreover, there is no objective reason to combine these references with the core group, much less any expectation of success in "decorating tumor cells with hapten" (instead of gene therapy) to elicit treatment for cancer.

In summation, this group of references contain no more incitement to the claimed invention by virtue of Sanda or Moody. For the foregoing reasons, the Examiner's rejection is overcome and should be withdrawn.

CONCLUSION

Applicant respectfully requests entry of the foregoing amendment and remarks in the file history of the above-identified application. The claims as amended satisfy the requirements for patentability under 35 U.S.C. §§ 103 and 112 and are, therefore, in condition for allowance. If any issue remains of concern, the Examiner is requested to contact the undersigned by telephone. Early allowance of the claims is earnestly solicited.

Respectfully submitted,



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